

Claims 2 and 5-7 have been canceled. Claims 1, 3-4, and 8-17 remain for consideration. Applicants note with appreciation that claim 14 has been found free of prior art.

Applicants have amended claim 1 to more particularly point out the invention. Support for this amendment is found, for example, in the Specification at page 16, lines 22-31, and page 17, lines 5-8.

Rejections under Muller-Leirheim

The Examiner rejected claims 1, 2, 11, 15 and 16 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 4,828,563 to Muller-Leirheim (Muller-Lierheim).

Applicants submit that amended claim 1, and claims 11, 15 and 16 are not anticipated by Muller-Lierheim. The disclosure in Muller-Lierheim relates to bonding active groups on a polymer layer. See Muller-Lierheim, col. 3, lines 40-44. Muller-Lierheim schematically discloses potential bonding active groups for attaching growth factors. There is no disclosure in Muller-Lierheim regarding the ability of the growth factors to stimulate association of viable cells with the polymer when the growth factor is attached. In the present application, the association of the growth factors with the substrate is effective for stimulating association of viable cells with the substrate. See Specification, for example, Example 2.

Since Muller-Lierheim does not disclose the claimed invention, Applicants respectfully request the withdrawal of the rejections of claims 1, 11, 15 and 16 under 35 U.S.C. § 102(b).

Rejections under Guire

The Examiner rejected claims 1-3, 8, 9, 11, 12, 15 and 16 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,263,992 to Guire (Guire).

Applicants submit that amended claim 1, and claims 3, 8, 9, 11, 12, 15 and 16 are not anticipated by Guire. There is no disclosure in Guire regarding covalent bonding of growth factors to substrates using crosslinking agents or noncovalent bonding characteristic of antibody-antigen, specific binding protein-receptor and enzyme-substrate associations as claimed in this application. Guire discloses the use of linker molecules having photochemical and thermochemical reactive groups that are externally activated.

The present invention uses crosslinking agents for covalently bonding the growth factor to the substrate. Crosslinking agents are difunctional compounds in which each functional group reacts with the substrate. Crosslinking agents do not have to be externally activated.

Since Guire does not disclose the claimed invention, Applicants respectfully request the withdrawal of the rejections of claims 1-3, 8, 9, 11, 12, 15 and 16 under 35 U.S.C. § 102(b).

Rejections under Noishiki

The Examiner rejected claims 1-4 under 35 U.S.C. § 102(b) as being anticipated by EP 0742020 by Noishiki (Noishiki). The Examiner indicated that attachment of growth factors with glutaraldehyde was known and used in the prior art of Noishiki.

Applicants submit that amended claim 1 and claims 3 and 4 are not anticipated by Noishiki. According to the Manual

of Patent Examining Procedures (MPEP), ". . . for anticipation under 35 U.S.C. 102, the reference must teach every aspect of the claimed invention either explicitly or impliedly." MPEP 706.02(a). Applicants believe there has been a misunderstanding regarding the disclosure in Noishiki. There is no disclosure in Noishiki regarding covalent bonding of growth factors to substrates using crosslinking agents or noncovalent bonding characteristic of antibody-antigen, specific binding protein-receptor and enzyme-substrate associations as claimed in this application.

The prior art of Noishiki is related to use of glutaraldehyde to attach a bioabsorbable substance to the prosthesis, not a growth factor to the substrate as in the present application. See Noishiki, col. 4, lines 17-20. Bioabsorbable substances are indicated to be collagen, albumin or gelatin. See Noishiki, for example, col. 1, lines 46-49. The discussion in Noishiki regarding growth factors is related to attachment of growth factors to the bioabsorbable substance, not the substrate as in the present invention. See Noishiki, for example, col. 5, lines 41-46 and col. 6, lines 4-5.

Since Noishiki does not disclose the claimed invention, Applicants respectfully request the withdrawal of the rejections of claims 1 and 3-4 under 35 U.S.C. § 102(b).

Rejections under Bayne

The Examiner rejected claims 1, 5-9, 12, 13, and 15-16 under 35 U.S.C. § 102(b) as being anticipated by EP 0476983 to Bayne et al. (Bayne). The Examiner indicated that Bayne uses fibrin to associate the growth factor with the substrate.

Applicants submit that amended claim 1 and claims 5-9, 12, 13, and 15-16 are not anticipated by Bayne. There is no disclosure in Bayne regarding covalent bonding of growth factors to substrates using crosslinking agents or noncovalent bonding characteristic of antibody-antigen, specific binding protein-receptor and enzyme-substrate associations as claimed in this application.

Since Bayne does not disclose the claimed invention, Applicants respectfully request the withdrawal of the rejections of claims 1, 5-9, 12, 13, and 15-16 under 35 U.S.C. § 102(b).

Rejection over Muller-Lierheim in view of Weatherford

The Examiner rejected claim 13 under 35 U.S.C. 103(a) as being unpatentable over Muller-Lierheim in view of Weatherford. The Examiner indicated that Muller-Lierheim discloses attaching growth factors to implants but fails to teach attaching vascular endothelial growth factor (VEGF) to a substrate. The Examiner also indicated that Weatherford teaches that it was known to attach VEGF to similar implants. The Examiner indicated that it would have been obvious to one of ordinary skill in the art to attach VEGF to a Muller-Lierheim implant in order to promote vascular endothelial cells ingrowth thereon.

Applicants submit that Muller-Lierheim does not disclose attaching growth factors to substrates as claimed in amended claim 1. Applicants also submit that there is no teaching or suggestion in Muller-Lierheim when combined with Weatherford that results in the invention as claimed in claim 13.

There is no teaching or suggestion in either cited reference, alone or combined, related to covalent bonding using crosslinking agents or noncovalent bonding characteristic of antibody-antigen, specific binding protein-receptor and enzyme-substrate associations effective to stimulate association of viable cells with the substrate. The discussion in Muller-Lierheim is related to bonding on the polymer surface. Muller-Lierheim merely discloses some exemplary schematic illustrations for attaching growth factors. There is no teaching or suggestion in Muller-Lierheim that the attachment of the growth factor is effective for stimulating association of viable cells with the substrate. The discussion in Weatherford relates to the use of fibrin glue with VEGF and heparin. Weatherford is silent with respect to covalent bonding of VEGF to a substrate and its effectiveness for stimulating association of viable cells.

Since the combination of Muller-Lierheim and Weatherford does not teach or suggest covalent bonding of growth factors to substrates using crosslinking agents or noncovalent bonding characteristic of antibody-antigen, specific binding protein-receptor and enzyme-substrate associations effective for stimulating association of viable cells to the substrate as claimed in this application, Applicants respectfully request the withdrawal of the rejection of claim 13 under 35 U.S.C. § 103(a) as being unpatentable over Muller-Lierheim in view of Weatherford.

Rejection over Guire in view of Goldstein

The Examiner rejected claim 10 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,263,992 to Guire (Guire) in view of U.S. Patent No. 5,613,982 to Goldstein

(Goldstein). The Examiner indicated that Guire discloses the use of human tissue as the implant substrate material but fails to disclose the use of animal tissue therefor. The Examiner also indicated that Goldstein teaches that it was known to use porcine tissue for similar implants. The Examiner concluded that it would have been obvious to use porcine tissue as the tissue substrate of Guire.

Applicants submit that there is no teaching or suggestion in Guire when combined with Goldstein that results in invention as claimed in claim 10, dependent on amended claim 1. There is no teaching or suggestion in either cited reference related to covalent bonding using crosslinking agents or noncovalent bonding characteristic of antibody-antigen, specific binding protein-receptor and enzyme-substrate associations. The discussion in Guire is related to bonding using linker molecules having photochemical and thermochemical reactive groups that are externally activated. See Guire, Col. 4, lines 58-61. The discussion in Goldstein relates to the use of porcine tissue. Goldstein does not teach or suggest attaching growth factors to substrates.

Since the combination of Guire and Goldstein does not teach or suggest covalent bonding of growth factors to substrates using crosslinking agents or noncovalent bonding characteristic of antibody-antigen, specific binding protein-receptor and enzyme-substrate associations as claimed in this application, Applicants respectfully request the withdrawal of the rejection of claim 13 under 35 U.S.C. § 103(a) as being unpatentable over Guire in view of Goldstein.

Rejection over Bayne

The Examiner rejected claim 17 under 35 U.S.C. 103(a) as being unpatentable over EP 0476983 to Bayne (Bayne). The Examiner indicated that Bayne meets the claim language except for the sterilizing and packaging of the implant as claimed. The Examiner indicated that sterilizing and packaging of the medical materials for distribution has been known in the art.

Applicants submit that Bayne does not teach or suggest claim 17, dependent on amended claim 1. As discussed above, amended claim 1 is not anticipated by Bayne. Applicants submit that there is no teaching or suggestion in Bayne related to covalent bonding using crosslinking agents or noncovalent bonding characteristic of antibody-antigen, specific binding protein-receptor and enzyme-substrate associations.

Applicants submit that amended claim 1 is not obvious over Bayne and thus, claim 17, dependent on claim 1 is also not obvious. Applicants respectfully request the withdrawal of the rejection of claim 17 under 35 U.S.C. § 103(a) as being unpatentable over Bayne.

Claim objection

The Examiner objected to claim 14 as being dependent on a rejected base claim. Applicants submit that amended claim 1 is now allowable. Thus, Applicants respectfully request the withdrawal of the objection to claim 14.

CONCLUSIONS

Applicant submits that this application is in condition for allowance, and such action is respectfully requested. The Examiner is invited to telephone the undersigned

agent to discuss any questions or comments that the Examiner may have.

The Commissioner is authorized to charge any fee deficiency required by this paper or credit any overpayment to Deposit Account No. 23-1123.

Respectfully submitted,

WESTMAN, CHAMPLIN & KELLY, P.A.

By: Visala C. Goswitz
Visala C. Goswitz, Ph.D., Reg. No. 41,042
Suite 1600 - International Centre
900 Second Avenue South
Minneapolis, Minnesota 55402-3319
Phone: (612) 334-3222 Fax: (612) 334-3312

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